UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,516	12/16/2008	Walter Keith Jones	10738-103	7508

24256 7590 11/14/2011

DINSMORE & SHOHL LLP
1900 CHEMED CENTER
255 EAST FIFTH STREET
CINCINNATI, OH 45202

EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
11/14/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,516	JONES, WALTER KEITH	
	Examiner	Art Unit	
	WU-CHENG SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-17 and 19-33* is/are pending in the application.

5a) Of the above claim(s) *1,3,8-17 and 19-31* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *2,4-7,32 and 33* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Considered Declaration filed on 11/07/2011.

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on Nov. 07, 2011 has been entered.

The declaration signed by Walker Keith Jones filed on 11/07/2011 has been considered.

Claim 18 is cancelled. No claim is amended.

Claims 1-17 and 19-33 are pending in the instant application.

Claims 1, 3, 8-17, and 19-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 2, 4-7, 32 and 33 are currently under examination to the extent of elected species (i.e. domain being NF-κB specific recited in claim 6 and NF-κB transcription factor recited in claim 7).

This application 10/596,516 is a 371 of PCT/US2004/042950 filed on 12/20/2004 which claims benefit of 60/531,399 filed on 12/19/2003 and claims benefit of 60/574,131 filed on 05/25/2004.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 2, 4-7, 32 and 33 remain ejected under 35 U.S.C. 103(a) as being unpatentable over **Sharma et al.** (Sharma et al. Transcription factor decoy approach to decipher the role of NF-kappaB in oncogenesis, *Anticancer Research*, 16(1): 61-69, 1996) in view of **Dzau et al.** (US 2003/0186922, publication date 10/02/2003, filed on 04/25/2003, priority date 10/29/1993) and **Weintraub et al.** (Weintraub et al. Retinoblastoma protein switches the E2F site from positive to negative element, *Nature* 358(6383):259-61, 1992). Applicant's arguments filed on 11/07/2011 have been fully considered and found not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 5-15 of the office action mailed on 07/07/2011.

For the clarity of record, the rejection for the reasons of record advanced on pages 5-15 of the office action mailed on 07/07/2011 is reiterated below.

Claim 2 is directed to a transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule, wherein the concatemerized double-stranded oligonucleotide

molecule comprises comprising at least 10 end-to-end repeated copies of a domain, wherein each of said domains comprises comprising a nucleotide sequence that acts as a transcription factor decoy for a transcription factor, and wherein each of said domains comprises from about 10 to about 40 nucleotide base pairs.

Claim 4 is directed to the transcription factor decoy of claim 2, further comprising at least one tissue-specific promoter.

Claim 5 is directed to the transcription factor decoy of claim 2, wherein the transcription factor decoy is capable of blocking signaling and gene expression associated with pathogenesis.

Claim 6 is directed to the transcription factor decoy of claim 1, wherein the decoys are NF-κB-specific.

Claim 7 is directed to the transcription factor decoy of claim 2, wherein the transcription factor is selected from NF-κB.

Claim 32 is directed to the transcription factor decoy of claim 2, wherein the concatemerized double-stranded oligonucleotide molecule comprises at least 15 end-to-end repeated copies of a domain.

Claim 33 is directed to the transcription factor decoy of claim 2, wherein the concatemerized double-stranded oligonucleotide molecule comprises at least 20 end-to-end repeated copies of a domain.

With regard to the limitations of claims 2, 5, 6 and 7, **Sharma et al.** teaches that the NF-κB transcription factor complex participate in the induction of numerous cellular and viral genes, and the role of NF-κB in *oncogenesis* (See introduction and title). Sharma et al. teaches transcription factor decoy approach to decipher the role of NF-kappaB in oncogenesis. In an effort to decipher the role of homo- vs heterodimeric NNF-kappa B in regulating tumor cell growth, Sharma et al. used a decoy approach to trap these complexes *in vivo*. Using *double-stranded phosphorothioates* as a direct *in vivo* competitor for homo- vs heterodimeric NF-kappa B, Sharma et al. demonstrate that decoys more specific to RelA inhibit growth tumor cell growth

in vitro. Sharma et al. demonstrate that RelA, either as a homodimer or a heterodimer with some other members of the Rel family and not the classical NF-κB (RelA/NFKB1), is involved in the differential growth control of tumor cells (See abstract, Sharma et al., 1996). Sharma et al. further teaches that basis of transcription factor decoy (TFD) approach to inhibit transcription factor function *in vivo* (See Figure 1, shown below).

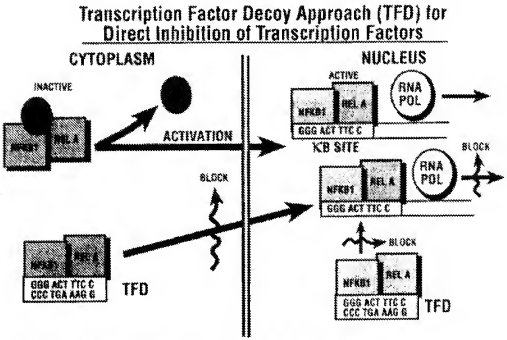


Figure 1. The Basis of the Transcription Factor Decoy (TFD) Approach to Inhibit Transcription Factor Function In Vivo.
Activation of the NF-κB transcription factor complex results in removal of IκB from the inactive complex, followed by nuclear translocation and transcriptional activation (left panel). In the presence of a TFD in the cytoplasm, the NF-κB complex can be sequestered by TFD prior to translocation, thus preventing nuclear translocation. A TFD in the nucleus can also bind to the active NF-κB complex, acting as a competitive inhibitor to block binding to cognate κB sites, thereby inhibiting transcription.

Sharma et al. teaches annealing the complementary stands *in vitro* in an annealing buffer to the NF-kB TFD sequences as follows:

5' GGG GAC TTT CCG CTG GGG ACT TTC CAG GGG GAC TTT CC 3'

It is noted that double-standed NF-κB TFD comprising ***three*** end-to-end repeated copies of consensus NF-kB binding site (5' GGG GAC TTT C 3'), which is 10 nucleotide base pairs.

Sharma et al. does not explicitly teach the limitations **(i)** "10 end-end repeated copies" recited in claim 2, "15 end-end repeated copies" recited in claim 32, and "20 end-end repeated copies" recited in claim 33, and **(ii)** further comprising at least one tissue-specific promoter recited in claim 4.

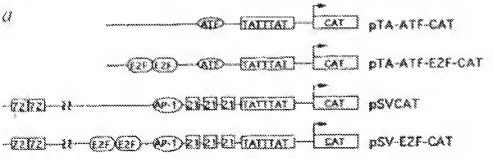
With regard to the limitations **(i)** "10 end-end repeated copies" recited in claim 2, "15 end-end repeated copies" recited in claim 32, and "20 end-end repeated copies" recited in claim 32, **Dzau et al.** teaches the use of oligodeoxynucleotide decoys for the prophylactic or therapeutic treatment of diseases associated with the binding of endogenous transcription factors to genes involved in cell growth, differentiation and signaling or to viral genes. By inhibiting endogenous trans-activating factors from binding transcription regulatory regions, the decoys modulate gene expression and thereby regulating pathological processes including inflammation, intimal hyperplasia, angiogenesis, neoplasia, immune responses and viral infection (See abstract, Dzau et al., 2003). Dzau et al. further teaches that the decoys contain sufficient nucleotide sequence to ensure target transcription factor binding specificity and affinity sufficient for therapeutic effectiveness. For the most part, the target transcription factors will require at least six base pairs, usually at least about eight base pairs for sufficient binding specificity and affinity. Frequently, providing the decoys with flanking sequences (ranging from about 5 to 50 bp) beside the binding site enhance binding affinity and/or specificity. Accordingly, *cis element flanking regions may be present and concatemer oligonucleotides may be constructed with* ***serial***

repetitions of the binding and/or cis element *flanking sequences* (See paragraph [0020], Dzau et al., 2003).

With regard to the limitation **(ii)** further comprising at least one tissue-specific promoter recited in claim 4, **Dzau et al.** teaches that the decoys may comprise a portion of a larger plasmid, including viral vectors, capable of episomal maintenance or constitutive replication in the target cell to provide longer term or enhanced intracellular exposure to the decoy sequence. Plasmids comprising *promoter* that regulates the expresses transcription factor decoy of interest are selected based on compatibility with the target cell (i.e. tissue specificity), size and restriction sites, replicative frequency, copy number maintenance, etc. For example, plasmids with relatively short half-lives in the target cell are preferred in situations where it is desirable to maintain therapeutic transcriptional modulation for less than the lifetime of the target cell (See paragraph [0021], Dzau et al., 2003).

Furthermore**, Weintraub et al.** teaches that the role of the E2F protein in *E1a* promoter activity was examined in transfection assays in which a competitor plasmid containing E2F binding sites was cotransfected with the plasmid pE1aCAT, which contains the E1a promoter fused to the gene for chloramphenicol acetyltransferase (*CAT*). This competitive binds and sequesters E2F, thus preventing it from interacting with the *E1a* promoter (See left column, page 259, Weintraub et al., 1992).

The diagram of the plasmids taught by Weintraub et al. in Figure 2a is shown below.



It is noted that there are multiple end-to-end transcription factor binding sites present in the promoter of double-stranded plasmid pTA-ATF-E2F-CAT and plasmid pSV-E2F-CAT.

Based on the combined teachings of Sharma et al., Dzau et al. and Weintraub et al., the ranges of the number of end-to-end repeats present in a NF-κB transcription factor decoy depend on the given cellular and viral genes to be inhibited in a given tissue in a desired *in vitro* experimental setting and/or intended *in vivo* therapeutic setting. The determination of the ranges of the number of end-to-end serial repeats present in a NF-κB transcription factor decoy is a process of optimization.

2144.05 [R-5] Obviousness of Ranges

See MPEP § 2131.03 for case law pertaining to rejections based on the anticipation of ranges under 35 U.S.C. 102 and 35 U.S.C. 102/103.

II. OPTIMIZATION OF RANGES

A. Optimization Within Prior Art Conditions or Through Routine Experimentation

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C

and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

B. Only Result-Effective Variables Can Be Optimized

A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.). See also In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) (prior art suggested proportional balancing to achieve desired results in the formation of an alloy).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Sharma et al. regarding the NF-κB transcription factor complex participate in the induction of numerous cellular and viral genes,

and the role of NF-κB in oncogenesis, transcription factor decoy approach to decipher the role of NF-kappaB in oncogenesis, and the double-stranded NF-κB TFD comprising three end-to-end repeated copies of consensus NF-κB binding site (5' GGG GAC TTT C 3'), which is 10 nucleotide base pairs, with the teachings of **(i)** Dzau et al. regarding *cis* element flanking regions may be present and concatemer oligonucleotides may be constructed with ***serial repetitions*** of the binding and/or *cis* element flanking sequences, and the decoys may comprise a portion of a larger plasmid, including viral vectors, capable of episomal maintenance or constitutive replication in the target cell to provide longer term or enhanced intracellular exposure to the decoy sequence, and **(ii)** Weintraub et al. regarding the role of the E2F protein in *E1a* promoter activity was examined in transfection assays in which a competitor plasmid containing E2F binding sites was cotransfected with the plasmid pE1aCAT, which contains the E1a promoter fused to the gene for chloramphenicol acetyltransferase (*CAT*), to arrive at claimed transcription factor decoy recited in claims 2, 4-7, 32 and 33 of instant application

One having ordinary skill in the art would have been motivated to combine the teachings of Sharma et al. with the teachings of Dzau et al., and Weintraub et al. because Sharma et al. teaches a functional role of NF-κB transcription factor in regulation of oncogenes is and using double-stranded NF-kB TFD comprising **three** end-to-end repeated copies of consensus NF-kB binding site (5' GGG GAC TTT C 3') whereas Dzau et al. specifically teaches that *cis* element flanking regions may be present and concatemer oligonucleotides may be constructed with ***serial repetitions*** of the binding and/or *cis* element flanking sequences, and Weintraub et al. teaches an example of promoter designed for analysis of retinoblastoma (RB) protein regulating E2F transcription factor binding to multiple E2F sites.

There would have been a reasonable expectation of success given (i) the successful demonstration of transcription factor decoy approach to decipher the role of homo- vs heterodimeric NNF-κB in regulating tumor cell growth, by the teachings of Sharma et al., (ii) successful demonstration of effect of decoy ODN (oligodeoxynucleotides) on *in vitro* and *in vivo* gene expression (See Examples 1-3), by the teachings of Dzau et al., and (iii) the successful demonstration of plasmids with multiple E2F transcription factor binding sites functioning as a transcription factor decoy that sequesters E2F transcription factor and thus preventing E2F transcription factor from interacting with the *E1a* promoter, by the teachings of Weintraub et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

The Examiner would like to direct Applicant's attention to recent decision by U.S. Supreme Court in *KSR International Co. v. Teleflex, Inc.* that forecloses the argument that a **specific** teaching, suggestion, or motivation is an absolute requirement to support a finding of obviousness. See recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1936) [available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf; and *KSR Guidelines Update* has been published in the Federal Register at 75 *Fed. Reg.* 53643-60 (Sep. 1, 2010) and is posted at USPTO's internet Web site at http://www.uspto.gov/patents/law/notices/2010.jsp]. The Examiner notes that in the instant case, even in the absence of recent decision by U.S. Supreme Court in *KSR International Co. v. Teleflex, Inc.,* the suggestion and motivation to combine the teachings of Sharma et al. with the teachings of Dzau et al. and Weintraub et al. has been clearly set forth above in this office action.

It is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's arguments

Applicant stated that Sharma does not recognize the number of end-to-end repeats as a result-effective variable. For example, Sharma gives no reasoning for the inclusion of three binding sites, does not compare the efficiency of that construct to a construct having fewer binding sites, and does not recognize the stabilizing effect of a greater number of end-to-end serial repeats. Thus, Sharma does not recognize the parameter - the number of serial repeats of a binding site - as a result-effective variable in a decoy.

Applicant stated that the Examiner has applied Weintraub for its asserted teaching of a promoter designed for analysis of E2F. However, as the Examiner noted, Weintraub is primarily directed to E2F gene promoters, rather than decoys blocking gene expression. Applicant finds no teaching or suggestion in Weintraub at all of a decoy, or of the benefit of designing a decoy having serial repetitions of a transcription factor binding site. The instant claims are directed to concatemerized transcription factor decoys, not promoters.

Applicant stated that Applicant further disagrees with the Examiner's interpretation of Dzau. However, to expedite prosecution, a signed 37 CFR §1.131 declaration swearing behind Dzau is submitted herewith. Dzau published October 2, 2003. The present application was filed December 16, 2008, and is a U.S. National Phase application of PCT/US2004/042950, filed December 20, 2004, which claims the benefit of U.S. Provisional Application No. 60/531,399, filed December 19, 2003, and U.S. Provisional Application No. 60/574,131, filed May 25, 2004. Accordingly, Dzau published less than one year before Applicant's earliest priority date, December 19, 2003.

Applicant stated that According to 35 U.S.C. §102(a), "[a] person shall be entitled to a patent unless ... the invention was ... described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent." When a prior publication is not a statutory bar, a 35 U.S.C. § 102(a) rejection can be overcome by antedating the publication date of the reference by submitting an affidavit or declaration under 35 U.S.C. § 1.131.

Applicant stated that pursuant to MPEP §715 and 37 CFR §1.131, an asserted reference may be sworn behind by demonstrating prior invention, which requires a showing of facts that, "establish reduction to practice prior to the effective date of the reference, or conception of the

invention prior to the effective date of the reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application."
Here, as shown in the signed 37 CFR 1.8131 declaration by the inventor, Walter Keith Jones, it is clear that the instant inventor conceived of the claimed subject matter prior to the publication date of Dzau and was diligent in his efforts until his constructive reduction to practice by virtue of the filing date of the U.S. Provisional Application No. 60/531,399, filed December 19, 2003. Accordingly, it is respectfully requested that Dzau be withdrawn from the above rejection as it is not a proper reference under 35 U.S.C. § 102(a).

Applicant stated that, in summary, the Examiner has conceded that Sharma does not teach all the claim elements, and has applied Dzau and Weintraub in his assertion that varying the number of end- to-end repeats of a binding site is mere optimization. Applicant submits Sharma does not teach or recognize this parameter as a result-effective variable, Weintraub is not directed to transcription factor decoys, and Dzau is not properly applied under 35 U.S.C. § 102(a) in view of the Declaration under 37 C.F.R. § 1.131 submitted herewith.

Response to Applicant's arguments

It is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

With regard to the arguments that "Weintraub is primarily directed to E2F gene promoters, rather than decoys blocking gene expression", it is noted that both Sharma et al. and Dzau et al. specifically teach decoys (i.e. verbatim) that can be used to titrate out the transcription factors that bind to a promoter. Furthermore, Weintraub et al. demonstrated that plasmids with multiple E2F transcription factor binding sites functions as a transcription factor decoy that sequesters E2F transcription factor and thus preventing E2F transcription factor from interacting with the *E1a* promoter (See Figure 4, page 262, Weintraub et al.).

With regard to the declaration signed by Walker Keith Jones filed on 11/07/2011, it is noted that **Dzau et al.** is US 2003/0186922 (application # 10/424,011, publication date

10/02/2003, filed on 04/25/2003), which is a CON of 08/524,206 filed on 09/08/1995, now US patent 6,774,118, which is a CON of 08/144,717 filed on 10/29/1993, now abandoned. Therefore, Dzau et al. is qualified as a prior under both 102(a) and 102(e). In light of the declaration filed by Walker Keith Jones on 11/07/2011, Dzau et al. is no longer qualified as a prior art under 102(a). However, Dzau et al. remains qualified as a prior art under 102(e).

Conclusion

2. No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/
Primary Examiner
Art Unit 1632